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# Deep venous thrombosis

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## Contents



## Aims

- To prevent pulmonary embolism and post-thrombotic syndrome.
- To actively look for thrombosis in risk groups.
- To prevent deep venous thrombosis in immobilized patients: calf muscle exercise, socks that prevent emboli, and, if necessary, prophylactic treatment with subcutaneous low-molecular-weight heparin (LMWH).
- A suspected deep venous thrombosis is verified by venography or compression ultrasonography.
- When the diagnosis has been confirmed in a hospital, the venous thrombosis can be treated at home (Level of Evidence=C; Evidence Summary available on the EBM Web site) or in a health centre. A distal deep popliteal thrombus does not cause emboli, and only about 20% of the thrombi reach the femoral level. -Idiopathic venous thrombosis may be a sign of a malignancy.

## Risk groups for deep venous thrombosis

- Acute immobilization, especially if the circulation is simultaneously impaired (heart insufficiency, surgery, infection, long flight)
- Trauma of the lower limbs (especially fractures in cast)
- Hereditary or acquired coagulation disturbances (See related EBM Guideline: **Leg oedema**

available on the EBM Web site) (always suspect these aetiologies when external causes for the thrombosis are not found)
- Polycythaemia, essential thrombocytosis
- Use of oral contraceptives, hormone-replacement therapy, especially in smokers
- A previous thrombosis
- Pregnancy and the postpartum period (6 weeks)
- Cancer in an active phase

# Symptoms

- Oedema of lower leg or calf (for differential diagnosis see related EBM Guideline: **Leg oedema** available on the EBM Web site)
- Tenderness or ache during rest
- Pain in the calf while walking
- Concurrent pain, tenderness and oedema strongly suggest deep venous thrombosis (59%). Each sign alone indicates thrombosis in only 11 - 22% of the cases (Level of Evidence=B; Evidence Summary available on the EBM Web site) [1].
- Often completely symptom-free, especially if the patient is in bed rest. The first symptom may be pulmonary embolism; in patients with hip fracture the thrombosis is often located in the femoral area only.

# Diagnosis

- The patient´s risk of thrombosis, or previous thrombosis, has an impact on the probability of the disease.
- Clinical findings
    - Oedema of the ankle and calf; in cases of thrombosis in the iliac vein oedema of the whole leg
    - Deep palpable tenderness over the involved vein
    - Positive Homans´ sign (not always, especially if the patient is in bed rest)
    - Warmth of the skin when compared with the other leg and prominent superficial collateral veins
- Doppler ultrasound examination:
    - Impaired flow in the popliteal vein when the calf is compressed
    - Impaired flow in posterior tibial veins when the pressure is relieved
    - In cases of ileofemoral venous thrombosis, the respiratory variation of the sound disappears, or the sound of spontaneous flow is weakened over the femoral vein in the groin.
- For differential diagnosis, see related EBM Guideline: **Leg oedema** available on the EBM Web site.

# How to act in cases of suspected deep venous thrombosis

- References[2, 3].
- The probability of venous thrombosis increases with the following signs and symptoms. (For each, give 1 point. If a diagnosis other than deep venous thrombus is very likely, subtract 2 points from the sum.)[1]
    - Cancer that is treated actively or that has metastasized

    - Paralysis or recent immobilization of a lower limb
    - Bed rest for more than 3 days
    - A major operation within 1 month
    - Local tenderness in the calf or in the thigh
    - More than a 3-cm difference in the circumference of the calves
    - Definite familial predisposition (at least 2 first-degree relatives with venous thrombi).
- The first investigation is nowadays **compression ultrasonography**, which is sensitive (90%) particularly in proximal thrombi, less sensitive (50%) in distal popliteal thrombi. Compression ultrasonography is replacing venography, which is useful in the diagnosis of recurrences.
    - An abnormal finding by ultrasonography is an indication for treatment. A normal finding in a low-risk patient (0 risk points) excludes venous thrombosis. A normal finding should be repeated in 7 days in a patient with moderate risk (1 - 2 risk points), and in a high-risk patient (3 points or more) venography should be performed immediately[3].
    - An abnormal venography (a constant intravenous filling deficit in at least two projections) is an indication for treatment. A normal finding excludes a venous thrombus.
- The **plasma D-dimer test** has been introduced as an exclusion examination (the test is very sensitive, but not as specific. A positive result does not therefore always indicate thrombosis).
    - If the plasma D-dimer is normal in a low-risk patient, other investigations are not needed[4].
    - If the first ultrasonographic finding and plasma D-dimer are both normal in a patient at a higher risk, repeated ultrasonography is not necessary[2].

# Treatment

## Basic rules

- In case of a proximal thrombus, early mobilization is recommended after a few days of heparin therapy.
- A distal and often also a proximal thrombus can be treated in a health centre or at home. Depending on the situation, the physician decides where the treatment will be carried out.
- Hospital treatment is indicated if there is
    - severe oedema of the whole lower limb
    - thrombus above the groin
    - other illnesses requiring hospital treatment.
- If the treatment is carried out at home, see that
    - the injection technique and drug dosage are correct
    - the follow-up of anticoagulation therapy is adequate
    - those who need a compression stocking will use it
    - possible complications are looked out for (bleeding, emboli).

# Choice of treatment according to the location and duration of the thrombus

- A high, ileofemoral thrombus or thrombus in the upper extremities with onset less than 7 days ago
    - Fibrinolysis with long-lasting (2 - 3 days) streptokinase treatment (Level of Evidence=B; Evidence Summary available on the EBM Web site); the contraindications are the

same as in fibrinolytic therapy for myocardial infarction. The aim is to decrease the risk of post-thrombotic syndrome. The use is limited to massive ileofemoral thrombi and haemodynamically dangerous pulmonary emboli[5].
    - LMWH (Level of Evidence=A; Evidence Summary available on the EBM Web site) has replaced i.v. heparin. Begin warfarin therapy concomitantly. **Heparin may be stopped when the INR has been in the target range (usually 2.0 - 3.0) for at least 2 days.**
    - Local fibrinolysis by catheterization.
    - Thrombectomy may be indicated if the vital functions of the lower limb are threatened.
- Distal thrombus in the lower extremities or any thrombus that is older than 7 days
    - LMWH (e.g. dalteparin 200 IU/kg/day) in 1 or 2 doses (Level of Evidence=A; Evidence Summary available on the EBM Web site). In patients susceptible to thombosis, two doses are recommended. Heparin may be stopped when after starting warfarin therapy the INR has been in the target range for at least 2 days. The treatment does not necessitate laboratory follow-up. In pregnant women and in patients with renal insufficiency, thrombophilia or haemophilia, the active concentration of heparin must be monitored. LMWH is at least as effective as ordinary heparin (Level of Evidence=A; Evidence Summary available on the EBM Web site) and causes less thrombocytopenia and paradoxical embolism.
    - Start warfarin therapy concomitantly with the heparin (see related EBM Guideline: **Oral anticoagulation therapy** available on the EBM Web site for instructions) and continue it for 2 - 6 months.
    - Bind the leg up with a bandage from the foot up to the upper thigh. The patient can stand up when the leg has been bound up.
    - Only about 25% of untreated distal thrombi proceed above the knee. Warfarin therapy is recommended, even though there is no consensus about the treatment of a popliteal thrombus[6].
- For the duration of warfarin therapy, see related EBM Guideline: **Vibration syndrome (vibration-induced white fingers)** available on the EBM Web site. -Prevention of deep venous thrombosis, see related EBM Guideline: **Prevention of venous thrombosis** available on the EBM Web site.

# Treatment of heparin-induced bleeding complications

- In heparin therapy-induced severe bleeding, the deficient blood products (fresh frozen plasma, thrombocytes) or protamine are given if unfractionated heparin has been used. Protamine is not as effective in reversing the action of LMWH and should be used with caution.

# Prognosis

- The risk of recurrence depends primarily on the underlying cause and its possible elimination. The duration of anticoagulation therapy is determined by the severity of the thrombosis and the risk of recurrence. In idiopathic thrombosis, the treatment time is often long, sometimes even life-long[7, 8].
- The condition of the venous valves is a major factor in the risk of post-thrombotic syndrome[7]. Anticoagulation therapy prevents the recurrence of the thrombus but does not protect the valves. On the other hand, a recurrence increases the risk of post-thrombotic syndrome many fold[9].
- The extent and, particularly, the high location of the thrombus have been considered risk factors for post-thrombotic syndrome, and in these cases thrombolysis therapy is aimed at

protecting the valves. This may be achieved by local thrombolytic therapy administered by catheterization[10]. However, this therapy is not readily available and may lead to complications, which is why each case must be assessed individually.
- A surgical (vai compressive) stocking reduced the risk of post-thrombotic syndrome and should always be worn[11].

# Related evidence

- Treatment of vitamin K antagonists reduces the risk of recurrent venous thromboembolism as long as it is used. However, the absolute risk of recurrence declines over time, while the risk of major bleeding remains (Level of Evidence=A; Evidence Summary available on the EBM Web site).
- Low-molecular weight heparins are equally effective and safer as vitamin K antagonists in the long-term treatment of symptomatic venous thromboembolism (but they are much more costly and need subcutaneous administration) (Level of Evidence=B; Evidence Summary available on the EBM Web site).
- The number of adverve events with low-molecular-weight heparin (LMWH) during pregnancy is small, but there are no RCTs comparing LMWH with unfractionated heparin (Level of Evidence=C; Evidence Summary available on the EBM Web site).
- The incidence of clinically overt venous thromboembolism in orthopaedic surgery patients with negative venography at discharge and no further pharmacological prophylaxis is less than 2% (Level of Evidence=B; Evidence Summary available on the EBM Web site).
- The ELISA method is more sensitive than latex test for D-dimer in the diagnosis of venous thromboembolism (deep venous thrombosis or pulmonary embolism) (Level of Evidence=C; Evidence Summary available on the EBM Web site).

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